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Title Page

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Abstract

Background: Anxiety is common after acute myocardial infarction (AMI) and has the potential to negatively affect physical and psychosocial recovery. There have been no cross-cultural comparisons of anxiety among AMI patients.

Aims: To evaluate whether anxiety after AMI differs across five diverse countries and to determine whether an interaction between country, and sociodemographic and clinical variables contributes to variations in reporting anxiety.

Methods and Results: A total of 912 individuals with confirmed AMI were enrolled in this prospective, comparative, cross-cultural study. Anxiety was assessed within 72 hours of hospital admission using the Brief Symptom Inventory. The mean level of anxiety in the entire sample was 0.62 ± 0.76, which is 44% higher than the normal mean level. Anxiety levels were not significantly different among the countries with the exception that patients in England reported lower levels of anxiety than those in the U.S. ($P = .03$). However, this difference disappeared after controlling for sociodemographic variables on which the countries differed.

Conclusion: Patients from each country studied experienced high anxiety after AMI. Even though various cultures were represented in this study, culture itself did not account for variations in anxiety after AMI. It appears that anxiety after AMI is a universal phenomenon. Given the potentially negative impact of anxiety on mortality and quality of life after AMI, clinicians and researchers should continue to explore interventions to treat anxiety and minimize its untoward effects.

1. Introduction

Ischemic heart disease affects people worldwide without regard to geographic location, socioeconomic status, or gender. According to the World Health Organization, over 7.1 million people die from ischemic heart disease each year. [1] Although it is well established that ischemic heart disease is the leading cause of mortality in Western countries, there has been an alarming increase in deaths from ischemic heart disease in developing countries. Therefore, experts predict that by the year 2020, over 11.8 million persons will die of ischemic heart disease annually, [2] which will make it the leading cause of death worldwide. [3]

Numerous investigators have studied the physiologic and emotional responses of patients from Western countries following acute myocardial infarction (AMI). [4-8] One such emotional response is anxiety, which has been defined as a "psychophysiological phenomenon experienced as a foreboding dread or threat to a human organism whether the threat is generated by internal, real or imagined dangers." [9] Investigators from North America reported that 10% to 26% of patients with AMI had higher levels of anxiety than patients with a psychiatric disorder. [6,10] However, the prevalence of anxiety after AMI has not been studied extensively among international populations. Additionally, to our knowledge, no investigators have evaluated whether the psychosocial or physiologic factors that are related to anxiety interact with the unique cultures within each country to produce a differential impact on anxiety.

Understanding anxiety from an international perspective is important because anxiety poses a significant risk to patients after AMI. This risk may result from activation of the sympathetic nervous system and hypothalamic-pituitary-adrenal (HPA) axis. [11] Investigators have shown that anxiety after AMI is associated with increased in-hospital complications such as lethal dysrhythmias, continued ischemia, and reinfarction. [6] Furthermore, anxiety has been

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shown to predict future coronary events and long-term survival after AMI. [5,7,8] However, individuals from different ethnic and cultural backgrounds may vary in their biological response to anxiety. [12]

People from all cultures and countries experience anxiety. [13] Furthermore, culture influences the perception of a stress-producing situation, symptoms of stress, and the expression of emotions. [14] Accordingly, the purposes of this study were to evaluate whether anxiety after AMI differs across five countries and to determine whether an interaction between country, and sociodemographic and clinical variables contributes to variations in the expression of anxiety. We previously reported that women had higher levels of anxiety than men in an international sample of AMI patients and noted that there were no differences in anxiety level across countries. [15] We conducted this secondary analysis to further explore this phenomenon.

2. Method

2.1. Design

This prospective, comparative, cross-cultural study was a substudy of a large international investigation of anxiety early after AMI. [15] In the current study we compared anxiety levels of participants with a diagnosis of AMI in five countries. The participants' state anxiety was assessed within the first 72 hours of hospital admission.

2.2. Participants and setting

Participants were recruited from community hospitals and academic medical centers from five countries – Australia, England, Japan, South Korea, and the United States (U.S.). Eligibility criteria for participation in this study included: 1) documented AMI by elevated cardiac isoenzymes and typical ECG changes; 2) onset of AMI outside of the hospital or other institutional setting, such as an extended care facility; 3) hemodynamic stability and absence of

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pain at the time of interview; and 4) intact cognitive function that allowed the participant to answer questions concerning their emotional status. Participants with life-threatening or debilitating co-morbidities were excluded from the study.

2.3. Procedures

The Institutional Review Board or its equivalent at each site granted permission to conduct this study and this investigation conformed with the principles outlined in the Declaration of Helsinki. All participants gave written informed consent after trained research assistants from each country explained the study to them. The research assistants were experienced cardiovascular nurses who collected data from each participant within 72 hours (mean 53 ± 38 hours) of admission to the hospital. During the interview, participants completed the Sociodemographic and Clinical Data Form and the Anxiety Subscale of the Brief Symptom Inventory. Some participants completed the instruments independently; however, most requested that the research assistants read the information to them. Additionally, clinical data were abstracted from the participant's medical record.

2.4. Measurement

2.4.1. Sociodemographic and clinical characteristics

The research assistants interviewed participants and evaluated their medical records to obtain the following sociodemographic and clinical data: age, education, gender, marital status, Killip classification, systolic and diastolic blood pressure on admission, pulse on admission, participant estimate of greatest intensity of chest pain prior to admission on a scale of 0 to 10 (0 = none; 10 = worst pain ever felt), medications used during hospitalization; and history of hypertension, diabetes, myocardial infarction, smoking, coronary artery bypass graft (CABG), percutaneous transluminal intervention (PTI).

2.4.2. Anxiety

We used the Anxiety Subscale of the Brief Symptom Inventory to measure state anxiety. Although concise, the 6-item subscale is a sensitive, reliable, and valid measure of state anxiety in acutely ill persons. [6,16] The Anxiety Subscale of the Brief Symptom Inventory was selected because it minimizes participant burden, is reliable and valid, and was conceptually relatively easy to translate from English to Korean and Japanese. Participants rate their level of emotional stress for each item on a scale of 0 to 4 (0 = "not at all" and 4 = "extremely"). The values for the six items are summed and averaged, with the averaged score representing the participant's overall level of state anxiety.

Native speaking researchers translated the Sociodemographic and Clinical Data Form and the Anxiety Subscale of the Brief Symptom Inventory from English into Korean and Japanese. A second native speaking researcher translated the instruments back into English to ensure that the translation process did not distort the meaning of the instruments. Reliability of the Anxiety Subscale was tested using Cronbach's alpha and were 0.88 for the Australian participants, 0.90 for participants from England, 0.87 for the Japanese participants, 0.90 for the South Korean participants, and 0.85 for the U.S. participants.

2.5. Statistical analyses

All data were entered into a personal computer and analyzed using SPSS software, version 11.5. Data are presented as frequencies and means ± standard deviations. To compare baseline differences in sociodemographic and clinical characteristics among countries, one-way analysis of variance (ANOVA) or chi-square were used as appropriate to the level of measurement. Multifactorial ANCOVA was used to evaluate whether there were differences in mean anxiety scores among the five countries while correcting for sociodemographic

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characteristics upon which the countries differed. Additionally, multifactorial ANCOVA was used to evaluate whether sociodemographic and clinical characteristics interacted with country to produce a differential impact on anxiety. A P-value of $< .05$ was considered statistically significant.

3. Results

3.1. Patient characteristics

A total of 912 AMI patients participated in this study; 127 from Australia, 144 from England, 136 from Japan, 128 from South Korea, and 377 from the U.S. Sociodemographic characteristics of the sample, by country are presented in Table 1. Patients' mean age at presentation with AMI in this study was similar among the countries with the exception that patients from South Korea were younger ($P < .02$). Patients from England and South Korea reported fewer years of education than patients from the remaining countries ($P < .004$). Substantially more patients in Japan and South Korea were married than patients from other countries ($P < .001$). Comparison of clinical characteristics among countries is reported in Table 2.

3.2. Anxiety levels among the countries

The mean level of anxiety in the entire sample was 0.62 ± 0.76, which is 44% higher than the normal mean level of 0.35. Levels in each country are illustrated in Figure 1. The mean levels of anxiety in each country were: 0.54 in Australia; 0.47 in England; 0.66 in Japan; 0.64 in South Korea; and 0.69 in the U.S. These levels are 54% higher than the normal mean anxiety level in Australia, 34% higher in England, 89% higher in Japan, 83% higher in South Korea, and 97% higher in the U.S. A total of 46%, 35%, 43%, 52%, and 50% of patients in Australia, England, Japan, South Korea and the U.S. respectively reported anxiety levels higher than the

norm reference mean. A total of 7%, 7%, 15%, 5%, and 10% of patients in Australia, England, Japan, South Korea and the U.S. respectively reported anxiety levels higher than the mean of 1.7 reported for psychiatric in-patients. [16]

Although there was a significant difference in anxiety level among the countries ($P = .03$) on the overall ANOVA, post hoc testing to discover where the countries differed using the Bonferroni test revealed that only England and the U.S. ($P = .03$) differed. Patients in England reported lower levels of anxiety than patients in the U.S. This difference in anxiety level disappeared after controlling for sociodemographic variables on which the countries differed.

3.3. Impact of interactions between country and sociodemographic and clinical variables on anxiety

The following sociodemographic and clinical characteristics were examined to determine if they interacted with country to influence anxiety: age, sex, marital status, education level, medical history, Killip classification on admission, use of various therapies in the emergency department and pain level. None of these variables interacted with country to affect anxiety. There was a main effect seen for sex and age, as we have previously reported. [15] Women and younger patients in each country reported higher levels of anxiety than men and patients older than 60 years.

4. Discussion

The principal findings from this study were that anxiety level early after AMI was high among patients from five diverse countries on four continents and did not differ substantially by country. Although, patients from England reported anxiety levels lower than those from the U.S., there were no differences among any of the other countries, and the difference between

English and U.S. patients disappeared after correction for sociodemographic variables on which the countries differed.

To our knowledge, this is the first cross-cultural comparison of anxiety levels in AMI patients early after the acute event. These findings demonstrate that, despite the potential influence of culture on emotion [14,17,18], patients suffering AMI display a similar emotional response to this potentially life-threatening event. If culture influences the experience, expression and communication of emotion, [19] why did we fail to find a difference in the expression of anxiety among patients from these five culturally diverse countries? Anxiety is thought to be a universal emotion found in all societies, but the expression and communication of anxiety are believed to be culturally different. However, Mesquita and Frijda, in a comprehensive review of cultural variation in emotions, [20] argue that there are little data from which one can conclusively argue that there are cultural variations in emotion. Depending on the theoretical framework from which one's view arises, there are data to support the notion that emotions are universal and data to support the notion that emotions are social constructs. [20] They further note that most of the research on cross-cultural comparisons of emotions considered only abstract representations of emotions and not concrete representations, such as the specific threat of physical illness. Thus, the expectation that there are cultural differences in the expression of anxiety may be unfounded.

Little cross-cultural research has been conducted to examine the emotions of patients after AMI. Scherer reported that among European, Japanese, and American university students, Japanese students were less fearful and more reserved about expressing their fear and exhibited a diminished physiological response to fear.[21] In contrast, others found that Chinese men who underwent cardiac catheterization and Taiwanese patients with AMI reported similar levels of

anxiety as American patients. [18,22]. In an epidemiologic review, Lepine pointed out that anxiety disorders are found in all countries that were studied. [13] Additionally, somatization of anxiety appears to be a common reaction across a variety of cultures. [14] Anticipation of physical danger has been reported as a precursor of anxiety in both non-Western and Western cultures. [20] Therefore, our finding that patients with AMI from five diverse countries expressed similar levels of anxiety suggests that the threatening nature of AMI produces anxiety regardless of the patient's culture.

The high anxiety level seen among patients in all countries is of concern for a number of reasons. The level of anxiety seen, even in patients from the country with the lowest mean anxiety level is substantially higher than that seen in healthy individuals. [16] For both humanistic and clinical reasons, it is essential to address this level of anxiety. Anxiety in cardiac patients is associated independently with higher short- and long-term morbidity and mortality. Patients with higher anxiety early after AMI have a longer stay in the cardiac care unit and hospital, [23,24] report sustained anxiety and long-term distress, suffer more symptoms irrespective of the severity of their physical condition, consume more health care resources, and report a lower quality of life than patients with lower anxiety.

We investigated the possibility that a number of clinical or sociodemographic factors that might affect anxiety level would interact with country to affect anxiety level. None of the multiple factors examined produced a differential effect on anxiety. This finding suggests that, among AMI patients, anxiety is common regardless of clinical presentation, presence of co-morbidities or severity of AMI, and that it can not be predicted by typical sociodemographic or clinical characteristics. Further research is warranted to determine factors that may moderate

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anxiety in order to better understand the phenomenon among AMI patients and develop effective interventions.

In summary, patients from each country studied experienced high anxiety after AMI. Even though various cultures were represented in this study, culture itself did not account for variations in anxiety after AMI. It appears that anxiety after AMI is a universal phenomenon. Given the potentially negative impact of anxiety on mortality and quality of life after AMI, clinicians and researchers should continue to explore interventions to treat anxiety and minimize its untoward effects.

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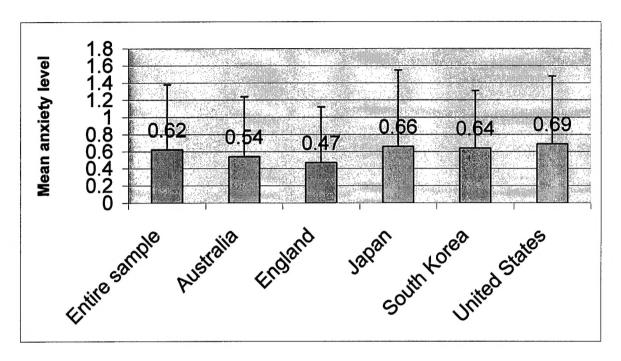
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Figure 1. Mean anxiety level among countries

Legend: Overall F test, $P = .03$; post hoc test reveal mean anxiety levels are significantly different between England and U.S ($P = .003$), and England and Japan ($P = .04$).

Table 1: Sample Sociodemographic Characteristics

Characteristic	Entire Sample	Australia	England	Japan	South Korea	United States
	N = 912	n = 127	n = 144	n = 136	n = 128	n = 377
Age, years*	61 ± 13	62 ± 13	61 ± 13	61 ± 11	57 ± 11	62 ± 14
Education, years**	12 ± 4	13 ± 4	10 ± 4	13 ± 3	11 ± 5	13 ± 3
Male***	658 (72.1)	101 (79.5)	111 (77.1)	109 (80.1)	99 (77.3)	238 (63.1)
Marital status						
Married@	684 (75)	87 (68.5)	108 (75)	117 (86)	117 (91.4)	255 (67.6)
Divorced/widowed/ single	220 (24.1)	40 (31.5)	33 (22.9)	19 (14)	10 (7.8)	118 (31.3)

Numbers are mean ± standard deviation or number (%); columns may not add to 100% because of missing data

* P = .02, South Korea < every other country; ** P = .004, England and South Korea < every other country; *** P = .001 U.S, < every other country; @ P = .001, Japan and South Korea > every other country

Table 2: Patient Clinical Characteristics

Characteristic	Entire Sample N = 912	Australia n = 127	England n = 144	Japan n = 136	South Korea n = 128	United States n = 377
Current smoker[*]	419 (45.9)	39 (30.7)	64 (44.4)	93 (68.4)	87 (68)	136 (36.1)
Hypertension[**]	482 (52.9)	48 (37.8)	59 (41)	74 (54.4)	62 (48.4)	239 (63.4)
Diabetes mellitus[***]	225 (24.7)	12 (9.4)	37 (25.7)	47 (34.6)	31 (24.2)	98 (26)
Previous AMI[**]	192 (21.1)	17 (13.4)	29 (20.1)	21 (15.4)	10 (7.8)	115 (30.5)
Killip class						
I[@]	604 (66.2)	99 (78)	104 (72.2)	116 (85.3)	78 (60.9)	207 (54.9)
II	229 (25.1)	21 (16.5)	29 (20.1)	13 (9.6)	37 (28.9)	129 (34.2)
III-IV	72 (7.9)	7 (5.5)	10 (7)	6 (4.4)	13 (10.2)	36 (9.6)

Treatment in ED						
Fibrinolytic[†]	310 (34.4)	34 (26.8)	99 (68.8)	20 (14.7)	36 (28.8)	121 (32.7)
Beta Blocker[‡]	320 (35.1)	28 (22.0)	72 (50.0)	11 (8.1)	10 (7.8)	199 (52.8)
Aspirin[§]	715 (78.4)	103 (81.1)	138 (95.8)	71 (52.2)	103 (80.5)	300 (79.6)
Anxiolytic[**]	270 (29.6)	30 (23.6)	43 (29.9)	28 (20.6)	33 (25.8)	136 (36.1)

Numbers are mean ± standard deviation or number (%); AMI = acute myocardial infarction; ED = emergency department

* $P = .001$, Japan and South Korea > every other country; ** $P = .001$, U.S. > every other country; *** $P = .001$, Australia < every other country; @ $P = .001$, Japan > every other country; † $P = .001$, England > every other country; ‡ $P = .001$, U.S. and England >

Australia > Japan and South Korea; § $P = .001$, England > U.S., Australia, South Korea > Japan

Australia > Japan and South Korea